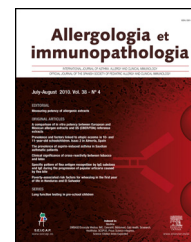




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ORIGINAL ARTICLE

Relationship between skin prick and atopic patch test reactivity to aeroallergens and disease severity in children with atopic dermatitis

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KEYWORDS

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Abstract

Background: The immunological mechanism in aetiology of atopic dermatitis (AD) shows significant differences from other allergic diseases. Allergen inhalation exacerbates AD lesions and AD patients' complaints decrease in house dust mite (HDM) low level environments, which reveals the importance of inhalant allergens.

Objective: We evaluated the skin prick test (SPT) and atopy patch test (APT) positivity rates with aeroallergens and studied the effect of test results, and aimed to determine the value of allergic test reactivity on the clinical characteristics of children with AD.

Methods: Forty-five children aged 2–15 years with AD were included to study between May 2006 and May 2007 in GATA Haydarpasa Teaching Hospital, Allergy Department. The reactivity to inhalant allergens using SPT and APT was evaluated. The severity of AD, which was assessed with SCORAD, was compared with aeroallergen hypersensitivity.

Results: The highest positivity of APT was seen against HDM (48.9%). HDM SPT positivity and subjective symptoms score were statistically correlated ($P < 0.05$). Patients with strong SPT positivity to HDM had a higher total SCORAD score ($P < 0.05$). Although there was no statistical correlation between HDM APT and SCORAD parameters, APT positive patients had generally higher SCORAD parameters. The statistical significance was only shown between the extent of the disease and strong APT positive reactions to *Dermatophagoides pteronyssinus*.

Conclusion: HDM allergens play an important role in determining the clinical severity of AD and strong APT positivity could be more meaningful clinically.

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Introduction

Atopic dermatitis (AD) affects children with a wide degree of severity. The immunological mechanism in aetiology of AD shows significant differences from other allergic diseases. Allergen exposure plays an important role in AD. Allergen inhalation exacerbates AD lesions and AD patients' complaints decrease in house dust mite (HDM) low level environments, which reveals the importance of inhalant allergens in AD.^{1,2}

It was shown that HDM are capable of inducing the release of multiple chemokines and pro-inflammatory cytokines from epidermal keratinocytes and dermal fibroblasts.³

The basic role of T lymphocyte in the physiopathology of AD lesions and its importance in late reactions^{4,5} brings forth the atopy patch test (APT) despite its controversial diagnostic value in clinical use.⁶

We evaluated the skin prick (SPT) and APT reactivity to aeroallergens and studied the relationship of test results to the clinical characteristics of children with AD.

Materials and methods

The study was approved by the local ethics committee, and written informed consent was given by the child's parents prior to enrolment.

Forty-five children aged 2–15 years with AD who applied to GATA Haydarpasa Teaching Hospital, Department of Allergy between May 2006 and 2007 were included in the study. All patients were tested using the prick test method with lancet. A standardised panel (ALK-Abello, Madrid, Spain) including HDM (*Dermatophagoides pteronyssinus* (Dp) and *Dermatophagoides farinea* (Df)), mould, grass, tree, weed, feather and dander mixed antigens were applied accompanied by positive (0.1% histamine phosphate) and negative (physiological serum: phosphate-buffered physiological saline) controls.

The resulting wheals were measured after 15 min. Positive reactions were defined as a wheal with a geometric mean diameter of at least 3 mm. Six mm and above were admitted as strong positive reactions.

After a week stopping antihistamines, systemic and topical corticosteroids, without exacerbation period in AD, aeroallergens in Vaseline (Stallergenes, Antony, France) with 12 mm aluminium chamber (Finn Chamber, Epitest Ltd Oy.) were used on the back of the patients for APT application.

HDM (Dp and Df), cat, dog, five grass mix, *Artemisia* and *Betula Alba* were used as aeroallergens. Pure Vaseline was used as negative control.

APT was read as follows⁷:

- Negative
- ? Only erythema, questionable
- + Erythema, infiltration
- ++ Erythema, few papules
- +++ Erythema, many or spreading papules
- ++++ Erythema, vesicles

Test materials were removed after 48 h. They were evaluated after 30 min from the removal time and re-evaluated

in 72 h. Three and four positive results were admitted as strong APT positivity.

A serum sample drawn on admission was analysed for total IgE. Total IgE was determined by using the microparticle enzyme immunoassay on the Imx analyser (Abbott park, IL, USA), according to the manufacturer's instructions. Serum levels above 120 IU/ml were admitted as high IgE value.

Patients diagnosed with AD before treatment were evaluated by the SCORAD index.⁸ The evaluation for each feature was made on an area with an average intensity symbolising lesions in general. Dryness was evaluated through non-inflamed skin.

Pruritus and sleep loss evaluation, containing at least the last three days and nights via 0–10 scale visual analogue scale, were used in the evaluation of subjective symptoms score.

Total SCORAD score is calculated using the Formula $\text{extent score}/5 + 7 \times \text{intensity score}/2 + \text{subjective symptoms score (Pruritus + sleep loss)}$. The severity of AD assessed with SCORAD was compared with SPT and APT reactivity to aeroallergens.

Statistical analysis

Statistical analyses were performed using SPSS 11.00 for Windows. Categorical data were analysed using Pearson chi-square test (Fisher exact test was used when needed), *P* value smaller than 0.05 was accepted as statistically significant. For some parameter relationships logistic regression analysis was used to evaluate the risk factors.

Results

45 patients, 21 (46.7%) male and 24 (53.3%) female, diagnosed with atopic dermatitis, were included in the study according to the Hanifin Rajka criteria. Mean age of the patients was 82.77 ± 43.76 (24–180) months. Average age of onset was 26.44 ± 28.8 (2–120) months. 25% of the patients were at or under the age of three. Mean duration of disease was 56 ± 41.1 (9–174) months.

SPT were positive in 68.9% of patients with aeroallergens. The HDM was the most common allergen (Fig. 1).

Highest reactivity of APT was seen against HDM (48.9%). Patch test reaction +++ and above was observed in nine (20%) patients to *D. pteronyssinus* and in eight (17.8%) patients against *D. farinea* (Figs. 2–4).

APTs of two patients (4.4%) showed irritant reaction to Vaseline (negative control). Various degree reactions (erythema and urticaria) regressing in 72nd hour to adhesive plaster were noticed in four (8.9%) patients. Whereas one patient who showed irritant reaction to the negative control did not show any reactions to other test materials, another patient showed reaction to all allergens; therefore APT was regarded as invalid.

Mean values were found as: SCORAD index 37.3 ± 12.13 (15.1–66.0), subjective symptom score 7.7 ± 4.07 (1–16), extent of disease 6.9 ± 5.41 (1–25), intensity score 8.1 ± 2.51 (3–14).

AD was accompanied by isolated rhinitis in 12 (26.7%) patients, isolated asthma in one (2.2%) patient and

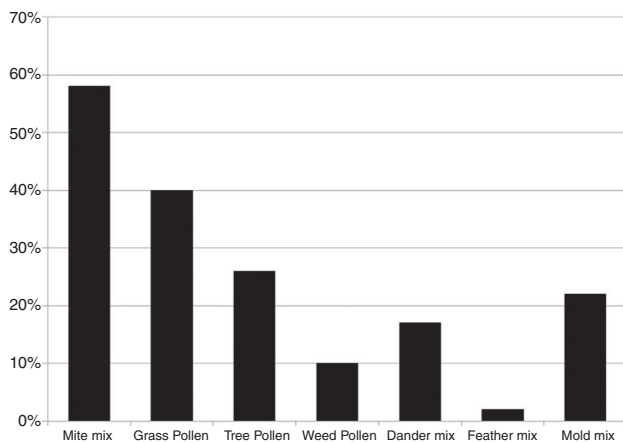


Figure 1 Skin prick test positivity of patients with aeroallergens.

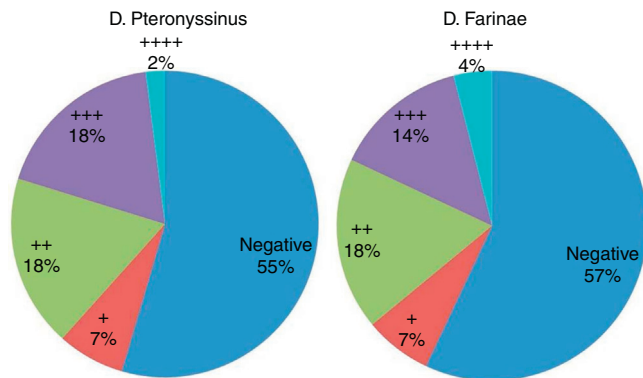


Figure 2 Atopy patch test results and rates with house dust mites.

rhinitis + asthma in 19 (42.2%) patients. AD was not accompanied by any respiratory atopic disease in 13 (28.9%) patients.

Whereas statistical relationship ($P=0.036$ and $P=0.05$) was found between the presence of respiratory disease associated with AD and sensitisation to inhalant allergens and IgE level, no relationship with patch testing was found.

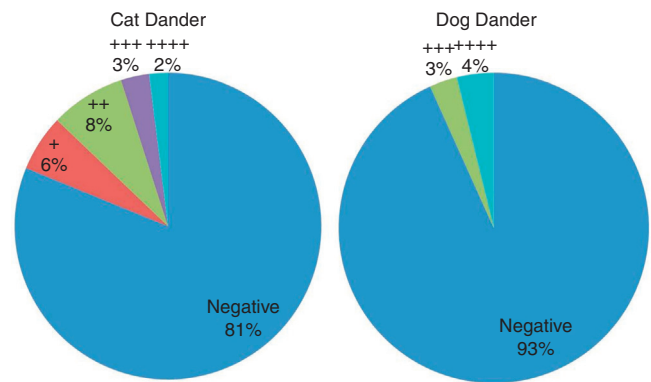


Figure 4 Atopy patch test results and rates with animal dander.

Correlation between HDM SPT positivity and strong APT positivity to Dp was found ($P=0.04$). The incidence of strong APT reaction to Dp and Df was also statistically high in patients showing strong SPT positivity to HDM ($P=0.016$ and $P=0.039$, respectively) (Table 1).

A positive relation was observed in the regression analysis of grass pollen between SPT and APT (OR = 0.42 (0.20–1.5) 95% CI, $P=0.01$).

Although there was no statistical correlation between HDM APT and SCORAD parameters, APT positive patients had generally higher SCORAD parameters.

The statistical significance was only shown between the extent of the disease and strong APT positive reactions to Dp (Table 2).

SCORAD score, subjective symptoms score, extent and intensity of AD were compared separately with allergic parameters (aeroallergens SPT positivity, IgE level and existence of rhinitis and asthma). Only HDM SPT positivity and Subjective symptoms score were statistically correlated ($P<0.05$). Moreover, patients with strong SPT positivity to HDM had a higher total SCORAD score and subjective symptoms score ($P<0.05$).

Even though no statistical relation was found between parameters, SCORAD scores were higher in all patients with SPT positivity to inhaled allergens. Although subjective symptoms were higher for patients with high IgE level, this was not statistically significant ($P=0.068$).

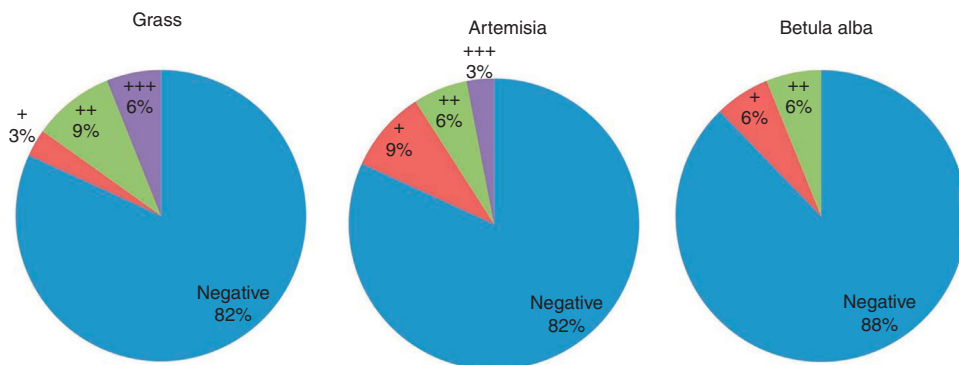


Figure 3 Atopy patch test results and rates with pollens.

Table 1 Correlation between strong SPT positivity to HDM and strong APT positivity to Dp and Df ($P < 0.05$).

	Strong APT positivity to Dp		Strong APT positivity to Df		Total
	Absent	Present	Absent	Present	
<i>Strong SPT positivity to HDM</i>					
Absent	24	2	24	2	26
Present	11	7	12	6	18
<i>Total</i>	35	9	36	8	44

Discussion

Rapidly developing symptoms (type-1 reactions) caused by allergens in allergic diseases can be easily diagnosed with detailed anamnesis, skin tests and/or specific IgE level measurements. However, diagnostic approaches are rather complex in late onset reactions, such as AD. The role of pollutants and allergens of the indoor air in the pathogenesis and clinical features of AD have not been investigated in detail.

It is reported that APT has a higher specificity than SPT and sIgE in the evaluation of aeroallergen-triggered AD flares.⁹ T cells obtained from AD skin lesions and allergen patch test area, responding selectively to *D. pteronyssinus* and other inhalant allergens, support the concept of forming an immune response on the skin of patients with AD with inhalant allergens.⁴

Positive patch test reaction ratios in AD patients differ between 15% and 70% in various studies.¹⁰ In a European multi-centre study in which AD patients were tested with different allergens, APT positivity ratios were variant between regions.¹⁰ The mean APT positivity to Dp was 39%, whereas regional APT positivity ratios were changed between 17 and 67% among the participant

countries. According to the conclusion of this study, APT results were only partially consistent with sIgE, SPT or patient history individually or in combination.¹⁰ In our study no relationship was observed between increased IgE levels and APT positivity to house dust mites. IgE molecule is considered to play a key role in the APT reaction or at least increase the severity.¹¹

In a study regarding AD severity and IgE level, a significant relation between SCORAD and serum IgE level was observed. It was found that patients with high SCORAD level were more often sensitive to inhalant allergens.¹² In our study we observed that AD being accompanied by diseases such as allergic rhinitis and asthma did not have an effect on SCORAD. None of the patients in the present study had a score over 75 points and only five patients had a SCORAD score over 50 points. It seems that lower SCORAD scores in our study might be related with different results with the previous study. Murat-Susić et al. reported a similar result to our study by showing that there is no correlation between serum IgE and eosinophil cationic protein level with severity of AD.¹³

Ingordo has compared HDM APT results with the severity of disease, in which no significant difference regarding SCORAD index could be found between HDM-APT positive and negative cases.¹⁴ Moreover, in another study while an

Table 2 Strong APT positivity to HDM and SCORAD parameters.

Strong APT positivity to Dp	Number	Strong APT positivity to Df	Number	Average scores	
				Dp	Df
<i>Total SCORAD index</i>					
Absent	35	Absent	35	36.09 ± 13.15	36.32 ± 13.36
Present	8	Present	8	42.15 ± 5.28	41.13 ± 3.65
Total	43	Total	43	37.22 ± 12.26	37.22 ± 12.26
<i>Subjective symptoms score</i>					
Absent	35	Absent	35	7.28 ± 4.36	7.37 ± 4.41
Present	8	Present	8	9.37 ± 2.19	9.00 ± 2.13
Total	43	Total	43	7.67 ± 4.11	7.67 ± 4.11
<i>AD extent</i>					
Absent	35	Absent	35	6.05 ± 5.47	6.28 ± 5.68
Present	8	Present	8	10.75 ± 3.61*	9.75 ± 3.37
Total	43	Total	43	6.93 ± 5.46	6.93 ± 5.46
<i>AD intensity</i>					
Absent	35	Absent	35	7.88 ± 2.69	7.91 ± 2.74
Present	8	Present	8	8.75 ± 1.58	8.62 ± 1.18
Total	43	Total	43	8.04 ± 2.53	8.04 ± 2.53

* $P < 0.05$.

inverse relationship was observed between Der p1 allergen exposure intensity with patch test reactivity in patients with AD, no correlation was found with SCORAD.¹⁵ In our study, strong APT reaction to Dp and Df was distinctively high in patients with strong SPT reactivity to HDM. It showed that strong allergy test positivity could reflect the severity of the disease better.

Our study shows that there is a significant correlation between HDM SPT positivity and subjective symptoms. In patients with strong positive SPT against HDM in addition to the subjective symptom score, total SCORAD score was also high. Strong APT positivity against Dp being found to be associated with the extensive AD shows that sensitisation to HDM allergens plays an important role in determining the clinical severity of AD and suggests that strong APT positivity could be more meaningful clinically. In recent years, it has been stated that HDM gained greater importance than foods in major causes of allergic AD¹⁶ and this conclusion is consistent with our study results.

In conclusion, our study results show that HDM sensitivity with higher scores of APT positivity had a direct effect on the extent of AD, and that HDM SPT positivity had an association with subjective symptoms of AD. Therefore APT and SPT tests have clinical importance in AD patients.

Ethical disclosures

Protection of human subjects and animals in research.

The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Conflict of interest

The authors have no conflict of interests to declare.

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